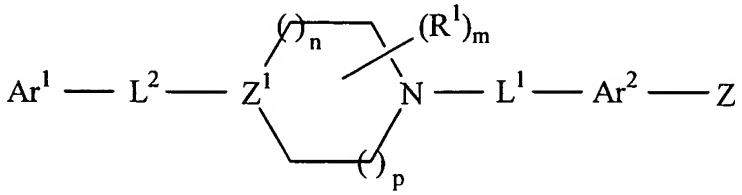
Abstract

The invention is directed to inhibition of p38-α kinase using compounds of the formula



and the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein:

Ar^1 is an aryl group substituted with 0-5 non-interfering substituents, wherein two adjacent noninterfering substituents can form a fused aromatic or nonaromatic ring;

L^1 and L^2 are linkers;

each R^1 is independently a noninterfering substituent;

Z^1 is CR^2 or N wherein R^2 is hydrogen or a noninterfering substituent;

m is 0-4;

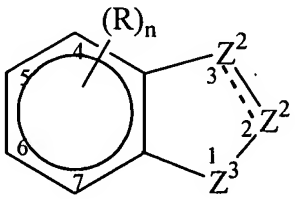
each of n and p is an integer from 0-2 wherein the sum of n and p is 0-3;

Ar^2 is a substantially planar, monocyclic or polycyclic aromatic moiety having one or more optional ring heteroatoms, said moiety being optionally substituted with one or more non-interfering substituents, two or more of which may form a fused ring;

Z is $-W_i-COX_jY$ wherein Y is COR^3 or an isostere thereof; R^3 is a noninterfering substituent, each of W and X is a spacer of 2-6 Å, and each of i and j is independently 0 or 1;

wherein the smallest number of covalent bonds in the compound separating the atom of Ar^1 bonded to L^2 to the atom of Ar^2 bonded to L^1 is at least 6, where each of said bonds has a bond length of 1.2 to 2.0 angstroms; and/or wherein the distance in space between the atom of Ar^1 bonded to L^2 and the atom of Ar^2 bonded to L^1 is 4.5-24 angstroms;

with the proviso that the portion of the compound represented by Ar^2-Z is not



wherein ⫽ represents a single or double bond; n is 0-3; one Z^2 is CA or CRA and the other is CR, CR_2, NR or N; A is $-W_i-COX_jY$ wherein Y is COR or an isostere thereof, each of W and X is a spacer of 2-6Å, and each of i and j is independently 0 or 1; Z^3 is NR or O; and each R is independently hydrogen or a noninterfering substituent.